

**REMARKS****A. Status of the Claims**

Claims 1, 4-13, 15-16, 18-37 and 39-66 are pending in this application with claims 6, 7, 29-36, 41-58 and 62-65 withdrawn from consideration. Claim 14 is cancelled. Claim 66 is newly added. Upon entry of these amendments presented herein, the claims under examination will be claims 1, 4, 5, 8, 9, 11-13, 15, 16, 18-28, 37, 39, 40, 59-61, and 66.

**B. Explanation of the Amendments**

Claims 1, 15-16, 18-21, 27-28, 37, 39, and 59 - 61 have been amended for clarification purposes. Support for the amendments may be found in the specification as filed, *see, e.g.*, Tables 1 and 2, *infra*. Applicants respectfully submit that no new matter has been added.

Table 1

| Claim Language  | Exemplary support in the Specification as filed  |
|---|--|
| 1. An immunogenic conjugate   | Title<br>Summary of the invention, p. 4 lines 2-3  |
| a protein and either a polysaccharide or an oligosaccharide   | p. 9 lines 10-16 (stating "The polysaccharide or oligosaccharide of this invention . . . conjugated to . . . a polypeptide or protein. Conjugation of the polysaccharide or oligosaccharide to the polypeptide. . .")    |
| wherein the protein is a bacterial or synthetic protein that comprises at least one lysine residue or at least one cysteine residue     | p. 9 lines 21-29<br><br>p. 9 line 21-25, p. 10 lines 3-5 (stating "The points of attachment are between lysine or cysteine residues of the protein and the N-acryloyl groups of the polysaccharide or oligosaccharide.") |
| wherein the polysaccharide or the oligosaccharide has been N-deacetylated and N-acryloylated to comprise at least one N-acryloyl group, | p. 4 lines 10-15, 20-23 (stating "A percentage of the N-acetyl groups are . . . replaced by N-acryloyl groups")  |

Table 1

|  |   |
|--|---|
| wherein the polysaccharide or the oligosaccharide is covalently attached to the protein via a $\beta$ -propionamido linkage between the at least one lysine residue or the at least one cysteine residue and at least one N-acryloyl group of the polysaccharide or oligosaccharide, and | <p>p. 4 lines 13-15 (stating “The N-acryloylated polysaccharide is directly coupled to a carrier protein to form the immunogenic <math>\beta</math>-propionamido-linked polysaccharide-protein conjugate.”)</p> <p>p. 4 lines 20-23 (stating “N-acryloyl groups . . . are directly coupled to protein to form the conjugate of the present invention”)</p> <p>p. 10 lines 3-5 (stating “The points of attachment are between lysine or cysteine residues of the protein and the N-acryloyl groups of the polysaccharide or oligosaccharide.”)</p> |
| wherein the polysaccharide or the oligosaccharide is derived from bacteria, yeast, or cancer cells, and  | <p>p. 5 lines 20-23 (stating “Polysaccharides or oligosaccharides may be obtained from . . . bacteria, yeast, or cancer cells.</p> <p>p. 11 lines 7-9 (stating “The polysaccharide may be derived from . . . bacteria, yeast, or cancer cells or from synthetic sources.”)</p>  |
| wherein the polysaccharide or the oligosaccharide is natural or synthetic  | <p>p. 11, line 7-12 (stating “The polysaccharide may be derived from . . . bacteria, yeast, or cancer cells or from synthetic sources. Synthetic sources include chemical synthesis, enzymatic synthesis and chemoenzymatic synthesis. The synthesis may be <i>de novo</i> synthesis or the modification of natural carbohydrates. Naturally isolated carbohydrates can be modified by altering functional groups on carbohydrate residues or by the addition or removal of carbohydrate residues.”)</p>  |

Table 2

| Claim amendment   | Exemplary support in the Specification as filed               |
|---|---|
| 16. An immunogenic conjugate produce by a method comprising | <p>Title</p> <p>Summary of the invention, p. 4 lines 4-15</p> |

Table 2

| Claim amendment  | Exemplary support in the Specification as filed   |
|--|---|
| removing about 50% of N-acetyl groups from either a polysaccharide or an oligosaccharide to form an N-deacetylated polysaccharide or an N-deacetylated oligosaccharide, wherein the polysaccharide or the oligosaccharide is derived from bacteria, yeast, or cancer cells, and wherein the polysaccharide or the oligosaccharide is natural or synthetic,   | p. 6 lines 12-17 (stating “In one embodiment, at least about 50% of the N-acetyl groups are removed... from the polysaccharide.”)<br>p. 7 line 24 to page 8 line 23 (providing methods of removing N-acetyl groups to form an N-deacetylated polysaccharide or N-deacetylated oligosaccharide).<br>p. 11 lines 4-12 |
| adding an acryloylating reagent to the N-deacetylated polysaccharide or the the N-deacetylated oligosaccharide to replace at least one removed N-acetyl group with at least one N-acryloyl group to form a N-acryloylated polysaccharide or an N-acryloylated oligosaccharide, and   | p. 4 lines 10-15, 20-23 (stating “A percentage of the N-acetyl groups are . . . replaced by N-acryloyl groups”)<br>p. 8 line 24 to p. 9 line 7 (discussing methods of N-Acryloylation of the Polysaccharide by adding an acryloylating reagent)   |
| conjugating the N-acryloylated polysaccharide or the N-acryloylated oligosaccharide with a bacterial or synthetic protein comprising at least one lysine residue or at least one cysteine residue to form a $\beta$ -propionamido linkage between the at least one lysine residue or at least one cysteine residue of the protein and the at least one N-acryloyl group of the N-acryloylated polysaccharide or the N-acryloylated oligosaccharide | p. 9 line 10 to p. 11 line 25 (discussing methods of conjugating an N-acryloylated polysaccharide with a protein and stating “The points of attachment are between lysine or cysteine residues of the protein and the N-acryloyl groups of the polysaccharide or oligosaccharide.”)                                 |

Newly added claim 66 finds support throughout the specification as filed, e.g.,

p. 4, lines 16-22, which states that

[c]apsular and cell surface polysaccharides can be extracted according to this invention from either bacterial, yeast, or mammalian cell supernatants or directly from bacterial, yeast or mammalian cells by hydrolysis of the base labile bond that connects the polysaccharide to other cellular components or by enzymatic hydrolysis. A percentage of the N-acetyl groups removed by hydrolysis from the polysaccharide are replaced by N-acryloyl groups, which in turn, are directly coupled to protein to form the conjugate of the present invention.

Claims 15, 18-21, 26 - 28, 39 and 59 - 61 have been amended to help ensure that the claim language of these dependent claims is consistent with amended claims 1 and 16.

Claim 37 has been amended to specify that the claimed polysaccharide- or oligosaccharide-containing vaccine “generates antibodies that are reactive against the bacteria, yeast or cancer cell from which the polysaccharide or the oligosaccharide was derived.” Support for this claim language is found on p. 12, lines 1-17 of the original specification, which states, inter alia, that “the isolated  $\beta$ -propionamido-linked polysaccharide-protein conjugates...may be used as an antigen to generate antibodies that are reactive against the polysaccharide or oligosaccharide and hence reactive against the organism or cell from which the polysaccharide or oligosaccharide was isolated.”

Applicants respectfully submit that no new matter has been added by these amendments. Furthermore, Applicants have not dedicated or abandoned any unclaimed subject matter, and have not acquiesced to any rejections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

C. The Claims Do Not Contain New Matter

Claims 1, 4, 5, 8, 9, 11-15, 16, 18-28, 37, 39, 40 and 59-61 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing new matter. In particular, the Examiner stated that the specification lacked support for a conjugate comprising a de-N-acetylated polysaccharide or de-N-acetylated oligosaccharide covalently attached to protein *without* N-acryloylation as previously claimed. *Office Action dated 5/19/2008*, at p. 4. Without acquiescing to the Examiner’s statement, Applicants respectfully direct the Examiner’s attention

to amended claim 1 and claim 16, wherein the polysaccharide or the oligosaccharide has been N-deacetylated and N-acryloylated to comprise at least one N-acryloyl group, and wherein the polysaccharide and the protein are coupled, e.g., covalently attached, to the protein via a  $\beta$ -propiionamido linkage between at least one lysine residue or at least one cysteine residue of the protein and at least one N-acroyl group of the polysaccharide or oligosaccharide. Support for the amendments may be found in the specification as filed, e.g., p. 4 lines 10-15, 20-23, p. 10, lines 3-5. Accordingly, the amendments do not add new matter.

The Examiner also suggested that the specification as filed provides no descriptive support for any 'protective antibodies', particularly for capsular polysaccharides or oligosaccharides of any source other than bacterial, yeast, or cancer cells. Further, the Examiner indicated that a step that comprises de-N-acetylating bacterial cell surface, yeast cell surface, or cancer cell surface lacks descriptive support. Without acquiescing to the Examiner's rejections, Applicants respectfully direct the Examiner's attention to the present claims 1 and 16, wherein Applicants have removed the claim language specifying that the conjugate elicits protective antibodies, and wherein it is clarified that it the polysaccharide or oligosaccharide that is N-deacetylated. Further, the amendments clarify that the polysaccharide or oligosaccharide is derived from bacteria, yeast or cancer cells. Support for this amendment may be found in the specification as filed, e.g., p. 5, lines 20-23. Further, Applicants respectfully indicate that a polysaccharide or oligosaccharide derived from bacteria, yeast or cancer cell includes those that are obtained naturally from the bacteria, yeast, or cancer cells themselves and those obtained synthetically via, e.g., *de novo* synthesis or modification of carbohydrates obtained from natural sources. See, e.g., *Specification*, at p. 11, lines 7-9. Further, Applicants respectfully assert that such polysaccharides or oligosaccharides derived from bacteria, yeast, or cancer cells include

capsular and cell surface polysaccharides derived from these sources. *See, e.g., Specification*, p. 4, lines 16-19. As such, Applicants have drafted new claim 66 to reflect such and assert that no new matter is added by this new claim. *See, e.g., Specification*, at p. 4, lines 16-19; *id.*, at p. 11, lines 7-9.

In view of the above remarks, Applicants respectfully request reconsideration and withdrawal of this rejection and the allowance of independent claims 1 and 16 and their corresponding dependent claims.

The Examiner also rejected claim 14 under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter. Without acquiescing to the Examiner's rejection, claim 14 has been cancelled. Applicants respectfully assert that cancellation of this claim renders the Examiner's rejection inapposite.

Claim 59 is rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing new matter. The Examiner contends that the phrase "reacting 'an...acryloyl moiety'" is not described in the specification as originally filed. Without acquiescing to the Examiner's allegations, claim 59 has been amended to make the claim language more consistent with that of claim 1. As such, Applicants respectfully assert that the Examiner's rejection has been rendered inapposite and should be withdrawn. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

Claim 37 and dependent claim 39 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing new matter. Without acquiescing to the Examiner's allegation and solely for the purpose of expediting prosecution, claim 37 has been amended as described above. In view of these amendments, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

D. The Claims Are Enabled

Claims 1, 4, 8, 9, 11-16, 18-28, 37, 39, 40 and 59-61 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled. In particular, the Examiner alleges that the specification does not enable an ordinarily skilled artisan to make and use a conjugate that elicits ‘protective antibodies’ reactive with the polysaccharide or oligosaccharide. Additionally, the Examiner rejects claims 25 and 40 as not enabled and alleges a “lack of showing that a de-N-acetylated or an N-acryloylated *Streptococcus* Group B polysaccharide- or oligosaccharide-tetanus toxoid conjugate can be combined with a second monovalent or multivalent protein component, such as, DTaP, or DTP, Td, DTaP-Hib, DTaP-IPV-Hib, or combinations thereof, wherein the conjugate still produces the required ‘protective antibodies’”.

As indicated above, the term “protective antibody” has been deleted from both claim 1 and claim 16, thereby rendering this ground of rejection moot. Claims 1 and 16 are now directed toward immunogenic polysaccharide-protein conjugates. Applicants respectfully assert that the specification as filed enables an ordinarily skilled artisan to make and use the claimed immunogenic polysaccharide-protein conjugate without undue experimentation. *See, e.g., Specification*, at pp. 7-11 and Example 1 (demonstrating how to make polysaccharide-protein conjugates); *see also id.*, at p. 12 lines 1-17 and Example 2 (demonstrating how to use the polysaccharide-protein conjugates). Furthermore, as explained in the specification as filed, such polysaccharide-protein conjugates are immunogenic, i.e., elicit an immune response, e.g., a T cell independent or a T cell dependent (e.g., antibody) response. *See, e.g., p. 9, lines 10-20 and Example 2.*

In light of the remarks above, Applicants respectfully assert that the claims are fully enabled. Accordingly, Applicants request reconsideration and withdrawal of this ground of rejection.

E. The Claims Are Definite Under 35 U.S.C. § 112, ¶ 2

Claims 1, 4, 5, 8-16, 18-28, 37, 39, 40 and 59-61 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite.

(a) The Office Action rejects Claim 1 for the following claim language, which is alleged to be indefinite and confusing: “wherein said de-N-acetylated polysaccharide or said de-N-acetylated oligosaccharide is derived from bacterial, yeast or cancer cell surface.” Applicants respectfully assert that in light of the claim amendments and remarks presented above, this rejection is inapposite. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

(b) The Office Action rejects Claims 1 and 16 for allegedly being unclear and for lacking antecedent basis for the term: “the polysaccharide” (line 9 of claim 1 and last line of claim 16). Applicants respectfully assert that in light of the claim amendments and remarks presented above, this rejection is inapposite. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

(c) The Office Action rejects Claims 4, 5, 11, 12 and 15 under the same basis of paragraph (b). Applicants respectfully assert that in light of the claim amendments and remarks presented above, this rejection is inapposite. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.



(d) The Office Action rejects Claim 16 for the following claim language, alleged to be vague and unclear: “reacting the N-acryloylated polysaccharide or the N-acryloylated oligosaccharide with protein...to form a  $\beta$ -propionamido linkage.” Applicants respectfully assert that in light of the claim amendments and remarks presented above, this rejection is inapposite. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

(e) The Office Action rejects Claim 26 for the following claim language, which allegedly improperly broadens the scope of the claim: “elicits an immune response specific to the polysaccharide or the oligosaccharide.” Applicants respectfully assert that in light of the claim amendments and remarks above, this rejection is inapposite. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

(f) Claim 37 was rejected for the following claim language, which is allegedly indefinite, confusing, and improperly broadening in scope: “member of a genus of an organism from which the polysaccharide or the oligosaccharide was obtained.” Applicants respectfully assert that in light of the claim amendments and remarks presented above, this rejection is inapposite. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

(g) The Office Action rejects Claim 39 for allegedly lacking proper antecedent basis for the term: “the bacteria”. Applicants respectfully assert that in light of the claim amendments and remarks presented above, this rejection is inapposite. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

(h) The Office Action rejects Claim 60 for containing the following phrase, alleged to be grammatically incorrect: “oligosaccharide N-acryloylated by at least 95%”.

Applicants respectfully assert that in light of the claim amendments and remarks above, this rejection is inapposite. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection..

(i) The Office Action rejects Claims 4, 5, 8-15, 18-28, 37, 40 and 59-61 for allegedly being indefinite. Applicants respectfully assert that in light of the claim amendments and remarks above, this rejection is inapposite. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

F. Claim Objections

The Examiner objects to Claims 1 and 16 for lacking a preceding article before certain claim terms. Applicants respectfully assert that these objections are moot in view of the claim amendments presented herein. Applicants therefore respectfully request reconsideration and withdrawal of the objections to these claims.

**CONCLUSION**

Based on the foregoing remarks, Applicants respectfully request withdrawal of the rejections of claims and allowance of this application.

**AUTHORIZATION**

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **50-3732**, Order No. **13564-105037**. In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **50-3732**, Order No. **13564-105037**.

Respectfully submitted,  
King & Spalding, LLP

Dated: November 12, 2008

By: /Joseph D. Eng Jr./  
Kenneth H. Sonnenfeld / Joseph D. Eng Jr.  
Reg. No. 33,285 / Reg. No. 54,084

Customer Number 65989  
**Correspondence Address:**  
King & Spalding  
1185 Avenue of the Americas  
New York, NY 10036-4003  
(212) 556-2324 Telephone  
(212) 556-2222 Facsimile